DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

FEB 23 2001

Jerome J. Klawitter, Ph.D.
President and CEO
Ascension Orthopedics, Inc.
8200 Cameron Road, Suite C-140
Austin, Texas 78754

Re: P000057
Ascension® MCP
Filed: February 20, 2001

Dear Dr. Klawitter:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed an initial review of your premarket approval application (PMA). We are pleased to inform you that we have made a threshold determination that the PMA is sufficiently complete to permit a substantive review and is, therefore, suitable for filing. The filing date is February 20, 2001, which is the date of CDRH receipt of the amended PMA.

We have also reviewed your request for expedited review of the PMA application. We believe that the Ascension® MCP may offer significant advantages in safety and effectiveness over existing alternatives; such as, increased biomechanical hand function and a lower rate of implant fracture. Therefore, we are pleased to inform you that your application will receive expedited processing.

You are reminded that it is imperative that the information used to support an application for expedited review meet the requirements of valid scientific evidence (21 CFR 860.7). This evidence would generally be obtained from well-designed, -monitored, and -controlled clinical trials so that the true merit of the medical device might be evaluated as promptly and efficiently as possible. You are further advised that the granting of expedited review status does not guarantee that the application will ultimately be approved.

Our review noted the following deficiencies and, in order to correct these deficiencies, we request the responses, as indicated:

1. As per your response, dated February 12, 2001, to items 1a and 2 of our letter dated February 9, 2001, please provide a statistical comparison to literature controls. Please include in your analysis as many primary and secondary parameters as possible (i.e., for which there are sufficient data);

2. Please provide patient labeling for your device. When developing your patient labeling submission, please refer to the attachment titled, "General Patient Labeling Recommendations;" and

3. In order to meet the requirements of 21 CFR Part 54, please provide financial disclosure information for the clinical investigators.

Please submit information addressing the above deficiencies in the form of an amendment to your PMA. In this amendment you may elect to correct the deficiencies or instruct CDRH to complete the review of your PMA and render a final decision on its approvability. You should recognize that a decision by you not to correct the above deficiencies may lead to an ultimate disapproval of your application. If you do not intend to address these deficiencies, please let us know as soon as possible.

This letter reflects the current progress of our administrative and limited scientific review of your application. Please be advised that the decision to file the PMA does not imply that either an in-depth evaluation of the safety and effectiveness of the device has been performed or a decision about the approvability of the application has been made. Rather, it represents a decision by CDRH that the application is sufficiently complete to begin the substantive review process. Further review of your application or any response to this letter may result in additional deficiencies.

In our initial review of your PMA, we noted that a patient in the United States received 3 Ascension® MCP implants between September 14, 1998 and July 31, 2000. Please be advised that since you have submitted a PMA for the Ascension® MCP and these devices do not meet all 5 of the criteria under the definition of a custom device (812.3(b), we do not consider this device to be a custom device. Therefore, we expect you to have an approved PMA or Investigational Device Exemption (IDE) before implanting additional devices in the United States.

Following receipt of a filing letter, an applicant is required by 21 CFR 814.20(e) to update its pending PMA 3 months after the filing date with new safety and effectiveness information learned about the device from ongoing or completed studies when the information may reasonably affect an evaluation of the safety or effectiveness of the device or may reasonably affect the statement of contraindications, warnings, precautions and adverse reactions in the draft labeling.

This updated reporting is limited to studies sponsored by the applicant or to which the applicant has reasonable access. The update report should be consistent with the data reporting provisions of the protocol. Please submit clinical updates in three copies as an amendment to the PMA and include the above PMA reference number assigned to the PMA.

The PMA cannot be approved until FDA has determined that the manufacturing facilities, methods and controls comply with the conditions set forth in your application and the applicable requirements of the Quality System Regulation (21 CFR Part 820). The document, Guidance For Preparation of PMA Manufacturing Information, that you received earlier, is based on the original Good Manufacturing Practice (GMP) Regulation. That regulation was superseded by the Quality System Regulation (QSR), which became effective on June 1, 1997.

The guidance document is currently under revision to conform with the additional requirements for design control established by the Quality System Regulation. Until the new guidance is available, you are not required to describe the design controls used for the PMA device. During the PMA inspection, however, you may be asked to demonstrate that any design operations for the PMA device, conducted after June 1, 1997, are in compliance with the design control requirements of 21 CFR 820.30.

If you have not already done so, please notify CDRH as soon as possible in the form of an amendment to the PMA if there will be a delay in setting up your manufacturing facility for production of the device, and provide the expected date that the facility will be prepared for an FDA inspection. If you have any questions regarding the status of your Quality System inspection please contact the Office of Compliance at (301)-594-4695, or your District Office.

A meeting of the Orthopedic and Rehabilitation Devices Panel will be held at which your PMA will be reviewed. You will be notified of the location and date of this meeting. Any additional information to be included in your PMA should be submitted in the form of a PMA amendment and be received by FDA at least 8 weeks in advance of the scheduled advisory panel meeting in order for FDA and the panel members to have adequate time to review the new information. Information received by CDRH less than 4 weeks in advance of a scheduled advisory panel meeting will not be considered or reviewed at the meeting and may delay consideration of your PMA until a subsequent advisory panel meeting.

For your information, there is an industry representative on this FDA advisory panel whose name, address and telephone number you can obtain by contacting the Committee Management Staff at (301) 594-1283. CDRH believes that industry representatives will be better prepared to participate in panel discussions if they have been provided with at least a copy of the Summary of Safety and Effectiveness Data for review prior to the panel meeting. In accordance with 21 CFR 14.86(b), all panel members are subject to all rules and regulations adopted by FDA and the committee; therefore, even though the industry representatives usually are not given access to trade secret and confidential, commercial information, they are bound to protect the confidentiality of documents that would be sent to them in preparation for panel review of a PMA. If you would like the industry representative to have access to any portion of your PMA, including the Summary of Safety and Effectiveness Data, please provide a copy to FDA for that purpose. Clearly identify the submission as a purged copy intended for review by the industry representative. Review of your PMA will not be prejudiced if you elect not to provide information for industry representative review.

As provided under 21 CFR 814.44(g), FDA will consider this PMA to have been voluntarily withdrawn if you fail to respond in writing within 180 days of the date of this request for a PMA amendment. You may, however, amend the PMA within the 180-day period to request an extension of time to respond. Any such request is subject to FDA approval and should justify the need for the extension and provide a reasonable estimate of when the requested information will

be submitted. If you do not amend the PMA within the 180-day period to (1) correct the above deficiencies, or (2) request an extension of time to respond and have the request approved, any amendment submitted after the 180-day period will be considered a resubmission of the PMA and will be assigned a new number. Under these circumstances, any resubmission will be given a new PMA number and will be subject to the requirements of 21 CFR 814.20.

All correspondence regarding this PMA should be submitted in 20 copies in the form of a PMA amendment. Please address all submissions to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions regarding this letter, please contact Mr. John S. Goode at (301) 594-2036 ext. 155.

Sincerely yours,

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative and
Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

GENERAL PATIENT LABELING RECOMMENDATIONS

When developing your patient labeling submission, you may wish to refer to FDA's draft Guidance *on Medical Device Patient Labeling*; you can find this document on our CDRH website:

http://www.fda.gov/cdrh/HumanFactors.html

We suggest that you use the draft Guidance and the related checklist provided in the Appendix of this document review whenever applicable. Many researchers who have studied what works well for information delivery have recommended the order of information provided in the draft Guidance. The draft Guidance provides seven pages of references to substantiate the research that went into our recommendations for presentation and content. Each item listed in the Appendix in this document review is discussed more extensively in the draft Guidance document.

We suggest you provide patient information about alternative treatments; such as fusion, and reasons why they are appropriate or not appropriate for his or her particular condition. What are the risks associated with the use of alternative treatments? (This type of information is provided on page 28 in the summary of safety and effectiveness.) What are the risks associated with the use of the Ascension device? (See page 20 in the safety and effectiveness section.)

We believe it would be helpful to give the patient an easy to understand description of the procedure. When a patient knows what to expect, he or she is frequently more relaxed. Simple line drawing graphics of the device and of the procedure could accompany this description. There are excellent graphics provided on pages 16 and 18 in the summary of safety and effectiveness.

Information for the patient should include any necessary contraindications, warnings, precautions, and adverse reactions. This type of information is provided on pages 19 and 20 in the summary of safety and effectiveness.

We believe it would be helpful for the patient to know before surgery what to expect post operatively. The patient may be involved in postoperative care. We believe a description should be given of what postoperative care will be required of the patient. This could include such information as:

- Wound care,
- Elevation of finger to lessen pain and swelling,
- Need for splinting,
- Since the sutures will remain in place for several days, the patient may need special instructions (e.g., keep the sutures dry?),
- Need to exercise the joint,
- Need to limit the stress on the device,
- What symptoms experienced that would warrant contacting the physician, and
- Possibility of repeated follow-up visits with the physician.

We suggest providing a section in the patient labeling on expected results after the surgery that might include:

- Range of motion,
- Range of pain usually experienced after a successful implantation,
- How long experienced pain may persist,
- How long the implant may last before needing to be replaced, and
- Possibility of revision, reoperation, fusion.

When the patient information is developed, we encourage you to test it on a representative sample of prospective users to assure that they will be able to understand it.

APPENDIX

CHECKLIST: RECOMMENDED ORDER OF PRESENTATION OF INFORMATION

- **Table of Contents**

- **Descriptive Information**
- Purpose of the Device:
- Description of the Device:
- Contraindications:
- Risks/Benefits:
- Expectations of the Device
- General Warnings and Precautions
- Procedure Associated with the Device:
- Alternative Devices and Procedures:

- **Additional Information**
  After the above information has been covered in the patient labeling, then you may, as desired, provide any other relevant information such as adverse events, clinical studies, comparative information, controversy, warranty, etc.

- **Index/Glossary**
  If a glossary is used or not used, all technical and medical terms should be defined as they appear in the text. If used, the Glossary should be placed after the Table of Contents to alert readers that it is there to help them. An index is needed if the labeling is lengthy or complex.

- **Printing Date**
  You should provide an obvious date of printing so the patient will know that the information provided is current. A printing date is required for prescription devices and recommended for all other devices.

- **User Assistance Information**
  You should provide a list of symptoms that would warrant a call to their surgeon if the patient experiences any of these symptoms. The applicant could provide a toll-free customer service telephone numbers.

OTHER ASPECTS OF LABELING TO CONSIDER

- **Readability**
- Reading level should be no higher than 8th grade, average reading level among adults
- Use one of readability formulas (manual or software) available to estimate reading level
- Test with a sample of likely users

- **Writing for increased comprehension**
- Write with a specific population in mind
- Stress need to know information
- Use concrete examples to clarify abstract ideas
- Organize sections in logical progression
- Define difficult terms/jargon
- Use active voice
- Use the personal pronoun "you" whenever possible
- Use short sentences
- Use bullets whenever possible

- **Appearance of text**
- Headings capture main points of text; questions are often good headings
- Use no smaller than 12 point type; 14 for older patients
- Serif font is easier to read; avoid glossy paper
- Highlight important points and use lots of white space, especially around important messages

- **Graphics**
- Please provide unshaded line drawings of the system of implants and any components; line drawings are clearer than photographs;
- Label clearly
- Avoid too many concepts within one graphic